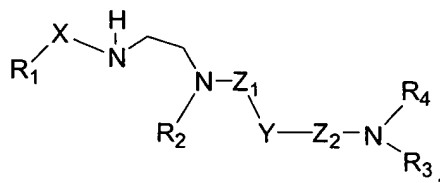


WHAT IS CLAIMED IS:

1. A method for treating an inflammatory or immune disease, a developmental or degenerative disease, or a tissue injury, comprising administering to a subject in need thereof an effective amount of a compound of the formula:



wherein

X is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, or deleted;

Y is aryl, heteroaryl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl, C_5 - C_8 heterocycloalkenyl, or deleted;

each of Z_1 and Z_2 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}=\text{CH}-$, $-\text{CH}=\text{N}-$, $-\text{CH}=\text{N}-\text{NR}-$, $-\text{S}-$, $-\text{O}-$, $-\text{NR}-$, $-\text{C}(\text{O})-$, or $-\text{SO}_2-$;

R_1 is H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl; C_5 - C_8 heterocycloalkenyl, aryl, or heteroaryl;

R_2 is $-\text{A}_1-\text{B}_1-\text{D}_1-\text{E}_1$;

R_3 is $-\text{A}_2-\text{B}_2-\text{D}_2-\text{E}_2$, deleted, or, together with R_4 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl; provided that if R_3 is deleted, $-\text{Z}_2-\text{N}-$ is $-\text{CH}=\text{N}-$; and

R_4 is $-\text{A}_3-\text{B}_3-\text{D}_3-\text{E}_3$ or, together with R_3 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl;

in which each of A_1 , A_2 , and A_3 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{C}_4\text{H}_8-$, $-\text{C}_5\text{H}_{10}-$, $-\text{CH}_2\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{CH}_2-$, $-\text{CH}_2\text{SO}_2-$, $-\text{SO}_2\text{CH}_2-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{CH}(\text{CH}_2\text{OR})-$, $-\text{CH}(\text{CH}_2\text{CH}_2\text{OR})-$, $-\text{CH}(\text{COOR})-$, $-\text{CH}(\text{CH}_2\text{COOR})-$, $-\text{CH}(\text{C}(\text{O})\text{NR}_2)-$, or deleted; each of B_1 , B_2 , and B_3 , independently, is $-\text{NR}-$, $-\text{CH}_2-$, or deleted; each of D_1 , D_2 , and D_3 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, $-\text{C}(\text{O})-\text{NR}-$, $-\text{C}(\text{S})-\text{NR}-$, $-\text{NR}-\text{C}(\text{O})-$, $-\text{NR}-\text{C}(\text{S})-$, $-\text{CH}(\text{OR})-$, $-\text{CH}(\text{CH}_2\text{OR})-$, $-\text{CH}(\text{CH}_2\text{CH}_2\text{OR})-$, $-\text{CH}(\text{COOR})-$, 1,1-cyclopropylene, or deleted; and each of E_1 , E_2 , and E_3 , independently, is H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_8 cycloalkyl, C_5 - C_8

cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl.

2. The method of claim 1, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, or -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

3. The method of claim 2, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

4. The method of claim 3, wherein X is -CH₂- or -CH(CH₃)-, Y is deleted, Z₁ is -CH₂-, and Z₂ is -CH₂-.

5. The method of claim 3, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

6. The method of claim 3, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.
7. The method of claim 3, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.
8. The method of claim 4, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄- or deleted; A₂ is deleted; A₃ is deleted; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl or heteroaryl; E₂ is H; and E₃ is aryl or heteroaryl.
9. The method of claim 5, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-, D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-, -CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.
10. The method of claim 6, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is -CH(CH₂OH)-; B₁ is -NH-; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is -CH₂- or deleted; D₃ is -CH₂-; E₁ is heteroaryl; E₂ is H or heteroaryl; and E₃ is aryl.
11. The method of claim 7, wherein R₁ is heteroaryl; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₃ is deleted; B₁ is -NH-; B₃ is -NH-; D₁ is -CH₂-; D₃ is -C(O)-; E₁ is heteroaryl; and E₃ is heteroaryl.
12. The method of claim 1, wherein the inflammatory or immune disease is asthma, allergic rhinitis, hypersensitivity lung disease, autoimmune disease, graft rejection, human immunodeficiency virus infection, or cancer.

13. The method of claim 12, wherein the cancer is brain, breast, prostate, colon, kidney, ovary, thyroid, lung, or haematopoietic cancer.

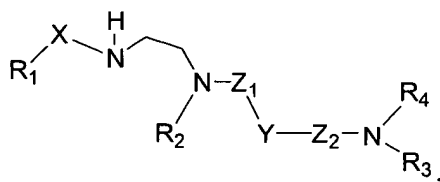
14. The method of claim 12, wherein the hypersensitivity lung disease is idiopathic pulmonary fibrosis.

15. The method of claim 12, wherein the autoimmune disease is rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, or systemic sclerosis.

16. The method of claim 1, wherein the developmental or degenerative disease is spinal muscular atrophy, Duchenne muscular dystrophy, Parkinson's disease, or Alzheimer's disease.

17. The method of claim 1, wherein the tissue injury is brain injury, heart injury, liver damage, skeletal muscle injury, kidney damage, pancreatic injury, lung injury, skin injury, or gastrointestinal tract injury.

18. A method for enhancing migration of bone marrow-derived cells to blood, comprising administering to a subject in need thereof an effective amount of a compound of the formula:



wherein

X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, or deleted;

Y is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, or deleted;

each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-, -CH=N-NR-, -S-, -O-, -NR-, -C(O)-, or -SO₂-;

R₁ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl;

R₂ is -A₁-B₁-D₁-E₁;

R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl; provided that if R₃ is deleted, -Z₂-N- is -CH=N-; and

R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl;

in which each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C₄H₈-, -C₅H₁₀-, -CH₂C(O)-, -C(O)CH₂-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, -CH(C(O)NR₂)-, or deleted; each of B₁, B₂, and B₃, independently, is -NR-, -CH₂-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -C(O)-NR-, -C(S)-NR-, -NR-C(O)-, -NR-C(S)-, -CH(OR)-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl.

19. The method of claim 18, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, or -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂,

and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

20. The method of claim 19, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

21. The method of claim 20, wherein X is -CH₂- or -CH(CH₃)-, Y is deleted, Z₁ is -CH₂-, and Z₂ is -CH₂-.

22. The method of claim 20, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

23. The method of claim 20, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.

24. The method of claim 20, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.

25. The method of claim 21, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄- or deleted; A₂ is deleted; A₃ is deleted; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl or heteroaryl; E₂ is H; and E₃ is aryl or heteroaryl.

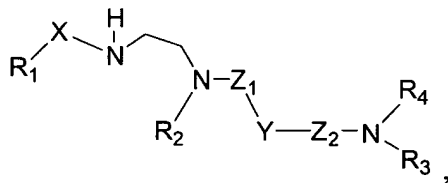
26. The method of claim 22, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-, D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-,

-CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.

27. The method of claim 23, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is -CH(CH₂OH)-; B₁ is -NH-; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is -CH₂- or deleted; D₃ is -CH₂-; E₁ is heteroaryl; E₂ is H or heteroaryl; and E₃ is aryl.

28. The method of claim 24, wherein R₁ is heteroaryl; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₃ is deleted; B₁ is -NH-; B₃ is -NH-; D₁ is -CH₂-; D₃ is -C(O)-; E₁ is heteroaryl; and E₃ is heteroaryl.

29. A compound of the formula:



wherein

X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, or deleted;

Y is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, or C₅-C₈ heterocycloalkenyl;

each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-, -CH=N-NR-, -S-, -O-, -NR-, -C(O)-, or -SO₂-;

R₁ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl; C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl;

R₂ is -A₁-B₁-D₁-E₁;

R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl; provided that if R₃ is deleted, -Z₂-N- is -CH=N-; and

R_4 is $-A_3-B_3-D_3-E_3$ or, together with R_3 , is C_4-C_{20} cycloalkyl, C_4-C_{20} cycloalkenyl, C_4-C_{20} heterocycloalkyl, or C_4-C_{20} heterocycloalkenyl; in which each of A_1 , A_2 , and A_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-C_4H_8-$, $-C_5H_{10}-$, $-CH_2C(O)-$, $-C(O)CH_2-$, $-CH_2SO_2-$, $-SO_2CH_2-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-CH(CH_2OR)-$, $-CH(CH_2CH_2OR)-$, $-CH(COOR)-$, $-CH(CH_2COOR)-$, $-CH(C(O)NR_2)-$, or deleted; each of B_1 , B_2 , and B_3 , independently, is $-NR-$, $-CH_2-$, or deleted; each of D_1 , D_2 , and D_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-C(O)-$, $-SO_2-$, $-C(O)-NR-$, $-C(S)-NR-$, $-NR-C(O)-$, $-NR-C(S)-$, $-CH(OR)-$, $-CH(CH_2OR)-$, $-CH(CH_2CH_2OR)-$, $-CH(COOR)-$, 1,1-cyclopropylene, or deleted; and each of E_1 , E_2 , and E_3 , independently, is H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, C_5-C_8 heterocycloalkenyl, aryl, or heteroaryl; each R , independently, being H or C_1-C_{10} alkyl.

30. The compound of claim 29, wherein X is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-SO_2-$, or deleted; Y is aryl, heteroaryl, C_5-C_8 cycloalkenyl; each of Z_1 and Z_2 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH=CH-$, $-CH=N-NR-$, $-NR-$, $-C(O)-$, or $-SO_2-$; R_1 is C_2-C_{10} alkynyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, aryl, or heteroaryl; R_3 is $-A_2-B_2-D_2-E_2$, deleted, or, together with R_4 , is C_4-C_{20} heterocycloalkyl or C_4-C_{20} heterocycloalkenyl; R_4 is $-A_3-B_3-D_3-E_3$ or, together with R_3 , is C_4-C_{20} heterocycloalkyl or C_4-C_{20} heterocycloalkenyl; each of A_1 , A_2 , and A_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2SO_2-$, $-SO_2CH_2-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, or $-CH(CH_2OR)-$, $-CH(CH_2CH_2OR)-$, $-CH(COOR)-$, $-CH(CH_2COOR)-$, deleted; each of D_1 , D_2 , and D_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-C(O)-$, $-SO_2-$, $-CH(OR)-$, $-CH(COOR)-$, 1,1-cyclopropylene, or deleted; and each of E_1 , E_2 , and E_3 , independently, is H, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, aryl, or heteroaryl.

31. The compound of claim 30, wherein X is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-SO_2-$, or deleted; Y is aryl or heteroaryl; each of Z_1 and Z_2 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH=CH-$, or $-SO_2-$; R_1 is C_3-C_8 heterocycloalkyl, aryl, or heteroaryl; each of A_1 , A_2 , and A_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2SO_2-$, $-SO_2CH_2-$, $-CH(CH_2OR)-$,

-CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

32. The compound of claim 31, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

33. The compound of claim 31, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.

34. The compound of claim 31, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.

35. The compound of claim 32, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-; D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-, -CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.

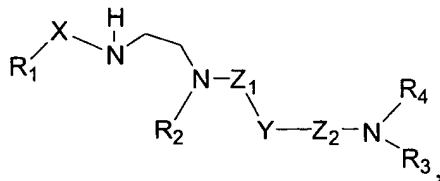
36. The compound of claim 35, wherein the compound is one of compounds 60-78, 80-84, 86-109, and 111-126.

37. The compound of claim 33, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is -CH(CH₂OH)-; B₁ is -NH-; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is -CH₂- or deleted; D₃ is -CH₂-; E₁ is heteroaryl; E₂ is H or heteroaryl; and E₃ is aryl.

38. The compound of claim 37, wherein the compound is compound 79 or 85.

39. The compound of claim 34, wherein R_1 is heteroaryl; R_4 is $-A_3-B_3-D_3-E_3$; A_1 is $-C_2H_4-$; A_3 is deleted; B_1 is $-NH-$; B_3 is $-NH-$; D_1 is $-CH_2-$; D_3 is $-C(O)-$; E_1 is heteroaryl; and E_3 is heteroaryl.

40. A compound of the formula:



wherein

X is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-SO_2-$, or deleted;

Y is aryl, heteroaryl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, C_5-C_8 heterocycloalkenyl, or deleted;

each of Z_1 and Z_2 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH=CH-$, $-CH=N-$, $-CH=N-NR-$, $-S-$, $-O-$, $-NR-$, $-C(O)-$, or $-SO_2-$;

R_1 is H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, C_5-C_8 heterocycloalkenyl, aryl, or heteroaryl;

R_2 is $-A_1-B_1-D_1-E_1$;

R_3 is $-A_2-B_2-D_2-E_2$, deleted, or, together with R_4 , is C_4-C_{20} cycloalkyl, C_4-C_{20} cycloalkenyl, C_4-C_{20} heterocycloalkyl, or C_4-C_{20} heterocycloalkenyl; provided that if R_3 is deleted, $-Z_2-N-$ is $-CH=N-$; and

R_4 is $-A_3-B_3-D_3-E_3$ or, together with R_3 , is C_4-C_{20} cycloalkyl, C_4-C_{20} cycloalkenyl, C_4-C_{20} heterocycloalkyl, or C_4-C_{20} heterocycloalkenyl;

in which each of A_1 , A_2 , and A_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-C_4H_8-$, $-C_5H_{10}-$, $-CH_2C(O)-$, $-C(O)CH_2-$, $-CH_2SO_2-$, $-SO_2CH_2-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-CH(CH_2OR)-$, $-CH(CH_2CH_2OR)-$, $-CH(COOR)-$, $-CH(CH_2COOR)-$, $-CH(C(O)NR_2)-$, or deleted; each of B_1 , B_2 , and B_3 , independently, is $-NR-$, $-CH_2-$, or deleted; each of D_1 , D_2 , and D_3 , independently, is $-CH_2-$, $-C_2H_4-$, $-C_3H_6-$, $-CH_2-CH=CH-$, $-CH=CH-CH_2-$, $-SO_2-$, $-C(O)-NR-$, $-C(S)-NR-$, $-NR-C(O)-$, $-NR-C(S)-$, $-CH(OR)-$, $-CH(CH_2OR)-$, $-CH(CH_2CH_2OR)-$, $-CH(COOR)-$, 1,1-cyclopropylene, or deleted; E_1 is H, C_1-C_{10} alkyl, C_2-

C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, 5-membered heteroaryl, fused heteroaryl, substituted 6-membered heteroaryl, unsubstituted pryanyl, unsubstituted pyrazinyl, unsubstituted pyrimidinyl, or unsubstituted pyridazinyl; and each of E₂ and E₃, independently, is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl.

41. The compound of claim 40, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, 5-membered heteroaryl, fused heteroaryl, or substituted 6-membered heteroaryl; and each of E₂ and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

42. The compound of claim 41, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; E₁ is H,

aryl, 5-membered heteroaryl, or fused heteroaryl; and each of E_2 and E_3 , independently, is H, aryl, or heteroaryl.

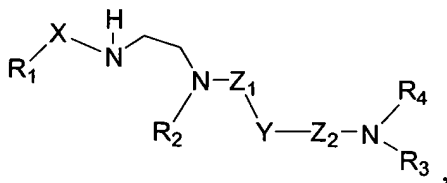
43. The compound of claim 42, wherein X is $-\text{CH}_2-$ or $-\text{CH}(\text{CH}_3)-$, Y is deleted, Z_1 is $-\text{CH}_2-$, and Z_2 is $-\text{CH}_2-$.

44. The compound of claim 43, wherein R_1 is aryl; R_3 is $-\text{A}_2-\text{B}_2-\text{D}_2-\text{E}_2$; R_4 is $-\text{A}_3-\text{B}_3-\text{D}_3-\text{E}_3$; A_1 is $-\text{C}_2\text{H}_4-$; A_2 is deleted; A_3 is deleted; B_1 is $-\text{NH}-$; B_2 is deleted; B_3 is deleted; D_1 is $-\text{CH}_2-$; D_2 is deleted; D_3 is $-\text{CH}_2-$; E_1 is aryl; E_2 is H; and E_3 is aryl.

45. The compound of claim 43, wherein R_1 is heteroaryl; R_3 is $-\text{A}_2-\text{B}_2-\text{D}_2-\text{E}_2$; R_4 is $-\text{A}_3-\text{B}_3-\text{D}_3-\text{E}_3$; A_1 is $-\text{C}_2\text{H}_4-$ or deleted; A_2 is deleted; A_3 is deleted; B_2 is deleted; B_3 is deleted; D_1 is $-\text{CH}_2-$; D_2 is deleted; D_3 is $-\text{CH}_2-$; E_1 is aryl, 5-membered heteroaryl, or fused heteroaryl; E_2 is H; and E_3 is heteroaryl.

46. The compound of claim 45, wherein the compound is compound 110.

47. A pharmaceutical composition comprising a compound of the formula:



wherein

X is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, or deleted;

Y is aryl, heteroaryl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl, C_5-C_8 heterocycloalkenyl, or deleted;

each of Z_1 and Z_2 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}=\text{CH}-$, $-\text{CH}=\text{N}-$, $-\text{CH}=\text{N}-\text{NR}-$, $-\text{S}-$, $-\text{O}-$, $-\text{NR}-$, $-\text{C}(\text{O})-$, or $-\text{SO}_2-$;

R_1 is H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, C_3-C_8 heterocycloalkyl; C_5-C_8 heterocycloalkenyl, aryl, or heteroaryl;

R_2 is $-\text{A}_1-\text{B}_1-\text{D}_1-\text{E}_1$;

R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl; provided that if R₃ is deleted, -Z₂-N- is -CH=N-; and

R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl;
 in which each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C₄H₈-, -C₅H₁₀-, -CH₂C(O)-, -C(O)CH₂-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, -CH(C(O)NR₂)-, or deleted; each of B₁, B₂, and B₃, independently, is -NR-, -CH₂-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -C(O)-NR-, -C(S)-NR-, -NR-C(O)-, -NR-C(S)-, -CH(OR)-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl; and
 a pharmaceutically acceptable carrier.

48. The composition of claim 47, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, or -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

49. The composition of claim 48, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

50. The composition of claim 49, wherein X is -CH₂- or -CH(CH₃)-, Y is deleted, Z₁ is -CH₂-, and Z₂ is -CH₂-.

51. The composition of claim 49, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

52. The composition of claim 49, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.

53. The composition of claim 49, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.

54. The composition of claim 50, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄- or deleted; A₂ is deleted; A₃ is deleted; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl or heteroaryl; E₂ is H; and E₃ is aryl or heteroaryl.

55. The composition of claim 51, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-, D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-, -CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or

heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.

56. The composition of claim 52, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is -CH(CH₂OH)-; B₁ is -NH-; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is -CH₂- or deleted; D₃ is -CH₂-; E₁ is heteroaryl; E₂ is H or heteroaryl; and E₃ is aryl.

57. The composition of claim 53, wherein R₁ is heteroaryl; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₃ is deleted; B₁ is -NH-; B₃ is -NH-; D₁ is -CH₂-; D₃ is -C(O)-; E₁ is heteroaryl; and E₃ is heteroaryl.